REMARKS

Claims 8-41, 63-64, 78-81 and 83-86 are pending in the application. Claims 8, 17, 39-40, 41, 63-64, 84-86 are here amended, and claim 82 is canceled. Applicants thank the Examiner for noting in the Office Action that claims 33-37 are free of the art.

Support for amendments to claim 8, 17, 39, 41, and 84-86 is found in the specification, e.g. on page 6, lines 3-5 and page 15, lines 10-11. Support for amendments to claim 63-64 is found in these claims and in claim 25 as originally filed. Support for amendments to claims 64 and 83 is found in claim 41 as originally filed. Support for amendments to claims 63-64 and 83 is found in those claims as filed. Claims 40, 63-64 and 83 are amended to correct clerical errors. No new matter is added. The Office Action is properly non-final because it raises new grounds of rejection.

Claims 8, 17, 39, 41, and 84-86 as here amended are directed to compositions that are biological molecules, i.e., the nucleic acid, polysaccharide, saccharide, lipid, antibody or non-biopolymeric small molecules, the compositions having been modified by being covalently bonded to compounds that are alkoxysilanes. Most important, the modified biological molecules following covalent bonding to the compounds are soluble in aqueous solution. The compositions and methods herein are reacted in aqueous solution, and remain in aqueous solution, and in this form are further used or stored for further use, *viz.*, the modified biological molecule compositions are printed on the solid supports to form microarrays. These molecules overcome the problems of the prior art, in which biological molecules are reacted directly with pre-treated solid supports. The claims as here amended are directed to subject matter which is entirely different from pre-treatment of solid supports, such pre-treatment being found in all of the cited prior art. Thus the present claims avoid the problems associated with pre-treated solid supports, *viz.*, that the supports can non-specifically react with components of a test sample added to the solid supports when these are later used for various purposes.

Issues under 35 U.S.C. § 112, ¶ 2

The Office Action on page 2, ¶ 3 rejects claims 17-23 for reciting, "alkoxysilane group soluble in solution.". Claim 17 as here amended is directed to a modified biological composition

that is soluble in aqueous solution. The claim as here amended satisfies 35 U.S.C. § 112, ¶ 2. Applicants respectfully request that this rejection of claim 17 and its dependent claims 18-23 be withdrawn.

Claims as amended are novel

Plueddemann et al., U.S. Patent Number 4,231,910

The Office Action on page 2, ¶ 4 rejects claims 8-9, 13-16 and 78 under 35 U.S.C. 102(b) as anticipated by Plueddemann. The Examiner alleges that Plueddemann teaches a nucleic acid (DNA) bound to a compound having the formula $R_1 — X — R_2$. Applicants traverse, and assert that in fact Plueddemann does not disclose any compositions that are modified biological molecules, such as nucleic acids, that are modified by being reacted covalently bonded with an alkoxysilane, let alone that the modified compositions are soluble in aqueous solution.

The Plueddemann abstract defines the term "primer compositions" in this reference as relating to plastic adhesion:.

> A primer composition consisting essentially of 75-99 percent alkoxymethyltriazine and 1 to 25 percent 3-glycidoxypropyltrimethoxysilane, 2(3,4-epoxycyclohexyl)-ethyltrimethoxysilane, 3-mercaptopropyltrimethoxysilane, 2-mercaptoethyltrimethoxysilane or a partial hydrolyzate of the silanes is employed to improve wet and dry adhesion of thermoplastics to solid substrate. [Emphases added]

The term "primer" is has different meanings in the field of plastic adhesion and in nucleic acid biochemistry. Plueddemann's "primer" is clearly not a nucleic acid of any kind, but a priming agent for use with a plastic adhesive.

Applicants assert that Plueddemann simply does not disclose any composition as described in claim 8, such as a nucleic acid covalently bound to a compound having the formula R_1-X-R_2 and that is soluble in aqueous solution. As Plueddemann is not the same as claim 8, therefore this reference does not anticipate claim 8. Claims 9, 13-16 and 78 depend directly or indirectly from claim 8, therefore claims 9, 13-16 and 78 are also not anticipated by Plueddemann.

Applicants respectfully request that rejection of claims 8, 9, 13-16 and 78 as anticipated by Plueddemann be withdrawn.

Gray et al., U.S. Patent Number 5,851,769

The Office Action on page 3, ¶ 4B rejects claims 39-40, 63-64, 82-84, and 86 under 35 U.S.C. § 102(e) as anticipated by Gray et al., U.S. patent number 5,581,769. Applicants traverse with respect to claims as here amended, for at least the reason that Gray does not show molecules that are the same as the modified biological molecules of the claims as here amended: Gray's molecules are not soluble in aqueous solution (as in claims 39 and 84-86 as here amended). Further, Gray refers only to compounds that have two or three groups that are the same (three or two methoxy or ethoxy groups) while the claims as here amended are directed to compounds having three groups that are different (claims 64 and 83), as explained below.

The Examiner alleges that Gray et al. refers to a compound having the formula $R_1 — X — R_2$, wherein R_1 is an amino group, R_2 is an alkoxysilane group and X is a linking moiety. Claims 39 and 86 as here amended are directed to a modified biological molecule covalently bound to a compound having the fromulat: $--HN-(CH_2)_n-Si(OR)_3$, wherein n = 3, 4, 5, 6, 7, 8, or 9, and wherein the modified biological molecule is per se soluble in aqueous solution.

Gray et al. does not refer to any such modified biological molecule which is soluble in aqueous solution. In contrast, Gray in column 19, lines 35-36 states, "It is believed that compounds which form an attachment to the solid support via one functional group and which produce an exposed amine group ($–NH_2$) as the second functional group promote the binding of nucleic acid molecules to solid supports to produce the desired results." [Emphases added] Gray et al. shows only chemical, non-biological compounds that are attached to a surface in a first step; then Gray attaches the biological molecule to the compound which was first attached to the surface, thereby binding only unmodified biological molecules to a previously derivitized surface. As Gray is not the same as claim 39, Gray does not anticipate claim 39.

Claim 40 depends from claim 39, and incorporates the limitations of claim 39. Gray et al. does not teach every limitation of claim 39 or 40, therefore, Gray et al. does not anticipate claims 39 and 40. Applicants request that this rejection be withdrawn.

Claims 63 and 84 as here amended are directed to R_2 which is an alkoxysilane group, and, R_1 which is required to be a cyclic ether group, not an amino group. The Examiner admits that Gray et al. teaches to a compound having the formula $R_1 — X — R_2$, wherein R_1 is an amino group, R_2 is an alkoxysilane group and X is a linking moiety. Gray et al. simply does not teach a compound having the formula $R_1 — X — R_2$, wherein R_1 is a cyclic ether group, R_2 is an

alkoxysilane group and X is a linking moiety as in present claims 63 and 84. As Gray et al. is not the same as claims 63 or 84, therefore, Gray et al. does not anticipate claims 63 or 84. Applicants request that this rejection be withdrawn.

Further, Gray et al. shows five compounds used to link a nucleic acid to a surface in two steps: first, attaching the compound to the surface, and then, attaching the nucleic acid to the compound. These compounds, listed in Gray on column 19, lines 44-48 are as follows: 3-aminopropyltriethoxysilane, 3-aminopropyltrimethoxysilane, 3-aminopropyldiisopropylethoxysilane, 3-aminopropyldimethylethoxysilane, and 3-aminopropylmethydiethoxysilane.

In contrast to these five compounds in Gray, each of which has two or three identical R groups, claims 64 and 83 as here amended are directed to compositions covalently bonded to a compound having a formula in which R_1, R_2, and R_3 are different. Thus the claims as here amended are directed to subject that is different from the compounds referred to in Gray et al. Applicants have canceled claim 82, so rejection of this claim is moot.

Gray et al. is not the same as the subject matter of claims 64 or 83 as here amended, therefore Gray et al. does not anticipate claims 64 or 83.

Applicants respectfully request that rejection of claims as anticipated by Gray et al. be withdrawn.

Beattie et al. U.S. Patent Number 6,426,183

The Office Action on page 4 ¶ 4C rejects claims 8-10, 12, 17-19, and 21 under 35 U.S.C. § 102(e) as anticipated by Beattie et al., U.S. patent number 6,426,183. Applicants traverse, as Beattie does not teach a biological molecule modified by reaction with a compound of the formula: $R_1 — X — R_2$, wherein R_1 comprises a cyclic ether group, R_2 comprises an alkoxysilane group, and X comprises a moiety chemically suitable for linking the cyclic ether group and alkoxysilane group. Further, Beattie's compounds are not soluble in aqueous solution.

The Examiner alleges that Beattie et al. teaches a compound having formula $R_1 — X — R_2$, such that R_1 is a cyclic ether group, more specifically, an epoxy group, on column 18, lines 52-65, and therefore, that Beattie anticipates claims 8-10 and 12. Applicants respectfully disagree.

Nowhere does Beattie et al. refer to a compound of the formula $R_1 — X — R_2$ such that R_1 is a cyclic ether, and that this compound is reacted with a biological molecule. Beattie actually shows a compound in column 18, lines 52-65, having formula $R_1 — X — R_2$, with R_1 being an amino group, R_2 a hydroxy group, and X a linker connecting R_1 and R_2. Further, this compound in Beattie is not bound to any biological molecule, rather, it is generated in a synthesis shown in FIG. 1.

> Introduction of a primary amine function onto the 3'-terminus of an oligonucleotide can be conveniently accomplished by the use of a special CPG support available from Clontech ('3'-Amine-ON^{TM}CPG ' or Glen Research ('3'-Amino-Modifier C3 CPG'). During post-synthetic incubation of this support in concentrated ammonia, the Fmoc protecting group is cleaved to generate function at the 3' end of the oligonucleotide, and a 3'-OH group is simultaneously generated by the cleavage of the succinate linkage to the glass. Since the pendant amine and hydroxy functions are on the carbon atoms 2 and 3 in the C3 linker, the resulting derivation is actually a 3'propanolamine or 3'aminopropanol. [Emphasis added]

This compound in Beattie is then, in a subsequent step, bound to an epoxy derivatized glass, which also is not reacted with a biological molecule.

As can be seen from these passages, the epoxy group in Beattie is never part of any compound having the formula $R_1 — X — R_2$ and that is reacted with a biological molecule, and therefore there is no epoxy group that is part of any biological molecule in Beattie.

Claim 8 is directed to a biological molecule modified by reaction with a compound having the formula: $R_1 — X — R_2$, wherein R_1 comprises a cyclic ether group, and is therefore not anticipated by Beattie et al. Further in claim 8, the composition bound to the compound is in aqueous solution, and for this reason also is not anticipated by Beattie et al.

Claims 9, 10 and 12 depend from claim 8, and so incorporate the subject matter of claim 8. Beattie et al. does not refer to this subject matter for any of the reasons described, therefore Beattie does not anticipate claims 8-10 and 12.

The Office Action rejects on page 4, ¶ 4C claims 17-19, and 21 as anticipated by Beattie et al. The Examiner asserts that Beattie et al. teaches biological molecules including oligonucleotides, peptides, polypeptides, proteins, hormones, antibodies, catalyst molecules,

carbohydrates and other organic molecules. Applicants traverse this rejection because Beattie et al. does not teach the subject matter of the claims as here amended.

Claim 17 as here amended is directed to a modified biological molecule that is reacted with a compound with a formula of $R_1 — X — R_2$, and the modified biological molecule is soluble in aqueous solution. Beattie et al. simply does not refer to any such modified biological molecule that is soluble in aqueous solution. Claims 18-19 and 21 depend from claim 17 and incorporate the limitations of claim 17. Therefore, Beattie does not anticipate claims 17-19 and 21.

Beattie et al. is not the same as and thus does not anticipate any of the claims as amended. Therefore, Applicants request that this rejection be withdrawn.

Rauh et al. U.S. Patent Number 5,401,415

The Office Action on page 4, ¶ 4D rejects claims 8, 11, 16-17, 20, 41 and 85 under 35 U.S.C. § 102(b) as anticipated by Rauh et al., U.S. patent number 5,401,415. Applicants traverse.

The Examiner alleges that Rauh et al. teaches a modified biological molecule covalently bound to a compound having the formula $R_1 — X — R_2$, wherein R_1 comprises a cyclic ether group or an amino group, R_2 comprises an alkoxysilane group, X comprises a linking moiety, and wherein the cyclic ether group is an epoxy group. The Examiner cites column 6, lines 26-67, and column 7, lines 15-52 of Rauh. Applicants respectfully disagree.

Claim 17 as here amended is directed to a modified biological molecule bound to a compound of formula $R_1 — X — R_2$ such that the modified biological molecule is soluble in aqueous solution. In Rauh et al., the compound cited by the Examiner is not soluble in any solution because it is attached to a glass bead. The beads with bound compound are exposed to cholesterol to bind the cholesterol to the bead. (*See* column 6, lines 26-67, and column 7, lines 15-52 of Rauh et al.).

Rauh does not refer to a biological molecule modified by reaction with a compound having the formula $R_1 — X — R_2$, wherein R_1 comprises a cyclic ether group or an amino group, R_2 comprises an alkoxysilane group, and X comprises a moiety for linking the cyclic ether group or the amino group to the alkoxysilane group, and the modified molecule is soluble in aqueous solution. While a molecule per se may be soluble in aqueous solution prior to an immobilization

of that molecule, that molecule when it is attached to a glass bead is immobilized to a solid phase matrix, and is part of the solid, and therefore is not in solution. The immobilized molecule may be solvated, but it is not in solution. In contrast, the modified biological molecules of the present claims remain soluble in aqueous solution after being modified as described in the present claims.

Claim 20 depends from claim 17 and therefore Rauh et al. anticipates neither of claims 17 and 20. Therefore, Applicants request that the rejection of these claims as anticipated by Rauh be withdrawn.

Claims 8, 11, 16, 41 and 85 are rejected under 35 U.S.C. § 102 as anticipated by Rauh et al. Applicants traverse.

Rauh et al. at column 13, line 54 to column 14, line 29, refers to a regeneration technique, in which derivatized glass beads are bound to cholesterol, and the cholesterol is then removed by washing with 6 M urea, so that the beads can be re-used and more cholesterol can be bound. Urea is used to dissociate non-covalent bonds such as hydrophobic interactions and hydrogen bonds. The lipid in Rauh et. al. is not modified as required by the present claims because it is not soluble in aqueous solution, and is it covalently bound to the compound having the formula $R_1 — X — R_2$.

Claim 8 is directed to a composition covalently bound to a compound having the formula $R_1 — X — R_2$. Claims 41 and 85 are directed to a modified biological molecules also covalently bonded to a compound, in the case of claim 85 further covalently bonded to a microarray comprising such modified biological molecules.

Rauh et al. does not refer to a composition covalently bonded to a compound having the formula $R_1 — X — R_2$, nor to a or a microarray comprising such covalently bound modified biological compositions. Therefore, Rauh et al. does not anticipate claims 8 and its dependent claims 11 and 16, nor claims 41 and 85.

Therefore, Applicants request that the rejection of claims 8, 11, 16-17, 20, 41 and 85 in view of Rauh et al. be withdrawn.

Correspondence Address

Applicants request that the correspondence address for this application be changed, pursuant to the revocation/new power of attorney that was previously filed in this case on September 30, 2003. The new correspondence address was changed to:

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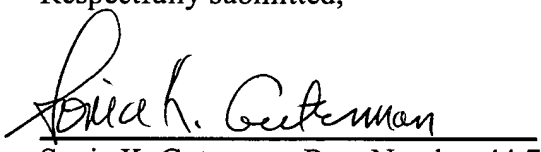
CONCLUSION

Applicants submit that the present claims are in condition for allowance, and such action is respectfully requested.

Should questions or issues arise concerning the application, the Examiner is invited and encouraged to contact the undersigned at the telephone number provided below.

Respectfully submitted,



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